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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,113	02/09/2001	John V. Tyrrell	506812000120	7970

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EXAMINER
MYERS, CARLA J

ART UNIT	PAPER NUMBER
1634	16

DATE MAILED: 01/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,113	TYRRELL ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-12,14,15,17-25,29-31,35,37,and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 16, 26-28, 32-34, 36, 39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Applicant's election with traverse of group 13, claims 13, 16, 26, 27, 28, 32-34, 36, 39, and 40 (with respect to SEQ ID NO: 15 and the pair of oligonucleotides of SEQ ID NO: 15 and 8) in Paper No. 15 is acknowledged. The traversal is on the ground(s) that it would not require undue burden to search each of the inventions together. This is not found persuasive because as indicated in the office action of Paper No. 14 undue burden would be required to examine all of the inventions together because this would require searching and evaluating 23 distinct nucleotide sequences.

The requirement is still deemed proper and is therefore made FINAL.

2. The disclosure is objected to because of the following informalities:

A. In claim 26, "ogligonucleotides" should be amended to read "oligonucleotides".

B. The specification is objected to because the assigned SEQ ID NOs have not been used to identify each sequence listed, as required under 37 CFR §1.821(d). See for example, pages 37 and 38 of the specification.

3. Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is indefinite because it is unclear as to what is intended to be encompassed by "one or more oligonucleotide" and it is unclear as to how claim 26 is intended to be further limiting from claim 13. It is unclear as to whether Y is to be one or more of the oligonucleotides

of the oligonucleotides listed in claim 13 (i.e. Y= one or more copies of SEQ ID NO: 15) or whether Y is one or more copies of any oligonucleotide.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13, 16, 26-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee (GenBank Accession No. AF042820).

Claims 13, 16 and 26 are drawn to oligonucleotides comprising SEQ ID NO: 15. Because of the open claim language "comprising", the claims include oligonucleotides which contain SEQ ID NO: 15 and any number of flanking nucleotides. Lee (GenBank Accession No. AF042820) teaches nucleic acids comprising the 24S large subunit ribosomal RNA sequence of *Heterosigma akashiwo*. The complementary inverse strand of this rRNA contains the 22 mer nucleotide sequence of SEQ ID NO: 15 (see nucleotides 127-149 of the rRNA of Lee). Accordingly, the oligonucleotide of Lee anticipates the invention of claims 13, 16 and 26. With respect to claims 27 and 28, the inverse complementary strand of the rRNA of Lee also contains the nucleotide sequence of the 22 mer of SEQ ID NO: 8 (see nucleotides 58-78 of the rRNA of Lee). The rRNA of Lee contains multiple copies of the rRNA nucleic acids and thereby Lee is

considered to teach compositions comprising the pair of oligonucleotides containing SEQ ID NO: 15 and SEQ ID NO: 8.

5. Claim 32 is rejected under 35 U.S.C. 102(b) as being anticipated by Asai (Nippon Kagakkai Koen Yokoshu, 1998, Vol. 75, page 315).

Asai teaches a method for detecting the raphidophyte *Heterosigma akashiwo*. In the method of Asai, the nucleic acids of *H. akashiwo* are released from the cell (which is considered to be a step of premeabilizing a cell to expose ribosomal RNA), the 18S rRNA sequences are hybridized with oligonucleotide primers and amplified by PCR (which is considered to be a step of contacting RNA with a probe capable of hybridizing to a hypervariable region) and the amplified PCR products are detected as indicative of the presence of a raphidophyte cell (which is considered to be a step of identifying hybridization complexes). Asai teaches that this method is useful for monitoring samples for the presence of the red tide phytoplankton *H. akashiwo* since this organism is associated with causing fish death.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32-34, 36, 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asai in view of Scholin (reference "22" cited in the IDS filed February 9, 2001) and Lee.

Asai teaches a method for detecting the raphidophyte *Heterosigma akashiwo*. In the method of Asai, the nucleic acids of *H. akashiwo* are released from the, the 18S rRNA sequences are hybridized with oligonucleotide primers and amplified by PCR and the amplified PCR products are detected as indicative of the presence of a raphidophyte cell. Asai teaches that this method is useful for monitoring samples for the presence of the red tide phytoplankton *H. akashiwo* since this organism is associated with causing fish death. Asai does not teach detecting *H. akashiwo* using a method of in situ fluorescent hybridization or a method of sandwich hybridization.

Scholin teaches methods for detecting microalgal species in environmental samples. Scholin teaches that microorganisms can be detected using either a fluorescent *in situ* hybridization methods or a sandwich hybridization method (see pages 192-193). The reference also teaches that these methods provide several advantages. In particular, the sandwich hybridization method a very rapid, easy and automatable means for detecting a microorganism and the fluorescent *in situ* hybridization method provides a means for analyzing the labeled cells

individually and for purifying labeled cells by cell-sorting flow cytometry (see page 195). The reference further teaches methods for identifying LSU rRNA probes useful for performing the detection methods and teaches that the LSU rRNA is useful as a probe because it contains hypervariable sequences and because rRNA is present in the cell at a high copy number, thereby increasing the sensitivity of the detection method. Scholin also teaches the reagents necessary to perform the disclosed hybridization method, including the reagent of hybridization buffer (see page 192-193). Additionally, the 24S rRNA sequence of *H. akashiwo* was known at the time the invention was made and is specifically taught by Lee.

In view of the teachings of Scholin and Lee, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Asai so as to have detected *H. akashiwo* using the sandwich hybridization or fluorescent in situ hybridization assay of Scholin in order to have provided an equally effective means for detecting *H. akashiwo* and to have provided sandwich hybridization methods which could be performed rapidly and in an automated format and to have provided fluorescent *in situ* hybridization methods which could be used to identify and isolate the positively labeled *H. akashiwo* cells. Additionally, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the 24S rRNA sequences of Lee comprising the 22 mer of SEQ ID NO: 15 as a probe since Scholin teaches that the LSU rRNA provides a useful probe for detecting microorganisms. While it is noted that the specification (page 36) teaches the improved results obtained when using probes consisting of SEQ ID NO: 15, the claims are

broadly drawn to probes and methods of using probes comprising SEQ ID NO: 15. Accordingly, these improved results do not apply to the claims as they are broadly written and, as discussed above, the prior art when considered as a whole would have lead one of skill in the art to detection methods using probes comprising SEQ ID NO: 15.

With respect to claims 39 and 40, Asai does not teach packaging oligonucleotides comprising SEQ ID NO: 15 and 8 into a kit. However, reagent kits for performing diagnostic methods were conventional in the field of molecular biology at the time the invention was made. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the *H. akashiwo* LSU rRNA probes and hybridization buffer in a kit for the expected benefits of convenience and cost-effectiveness for practioners in the art wishing to detect *H. akashiwo*.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

December 23, 2002

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER